EXHIBIT J

ADVISORY COMMITTEE ON ORGAN TRANSPLANTATION (ACOT)
U.S. Department of Health and Human Services (HHS)
Health Resources and Services Administration (HRSA)
Virtual Meeting
November 17, 2015, noon to 4 p.m.
LRG Offices, Washington, D.C.

ACOT Participants

Voting Members

Mark Barr, M.D.; Charles Alexander, R.N., M.S.N., M.B.A.; Sylvia Caley, M.B.A, R.N.; Bernice Coleman, Ph.D., R.N.; David Gerber, M.D.; Alexandra Glazier, J.D., M.P.H.; Ana Hands, M.D.; Eduardo Lara, B.A., M.H.A.; Arthur Matas, M.D.; Suzanne McDiarmid, M.D.; Jamie Marie Avolio McDonald, M.S.W., L.I.S.W.; Kimberly Molina, M.D.; Stephen Pastan, M.D.; and Cynthia Puryear.

Designated Federal Official

Patricia Stroup, M.B.A., M.P.A.

Welcome and Opening Remarks

Mark Barr, M.D., Chair, ACOT

Dr. Barr called the meeting to order at 12:15 p.m. and introduced Cheryl Dammons, associate administrator, Healthcare Systems Bureau, HRSA, HHS.

Ms. Dammons announced several staffing changes in the Division of Transplantation (DoT). Effective October 1, Dr. Melissa Greenwald assumed the role of acting division director. She had been working as a medical officer in the division for more than a year and has worked in the transplant arena for more than a decade. Previously, Dr. Greenwald worked in the Food and Drug Administration's (FDA) Office of Cellular Tissue and Gene Therapy. Ms. Dammons thanked Dr. Greenwald for stepping into her new position and encouraged all committee members to contact her whenever they need to do so.

Ms. Dammons also announced that Robert Walsh, who had served as the director of DoT, will serve as the division's senior advisor.

Finally, Ms. Dammons announced that effective November 2, Frank Holloman, M.P.A., began serving as deputy director/operations director for the DoT. Mr. Holloman joined HRSA after working at the National Institutes of Health (NIH) National Institute of Diabetes and Digestive and Kidney Diseases as chief of the office of management and policy analysis. In this role, he oversaw a multitude of programs, including Risk Management, Emergency Management, and the administration of wireless communication devices.

Program Report, DoT, HRSA

Melissa Greenwald, M.D., Acting Director, DoT

Dr. Greenwald began by announcing that, as of May 19, the Organ Procurement and Transplantation Network (OPTN) had reached an important milestone by having coordinated more than half a million transplants.

She mentioned that OPTN's kidney allocation system (KAS), which went into effect in December 2014, appears to be meeting expectations on a number of key outcomes.

Dr. Greenwald pointed out that much attention has been paid over the past few years to addressing disparities in liver transplantation. The most recent OPTN educational forum was held on June 22 to seek additional input on this issue, followed the next day by a meeting of the OPTN/United Network for Organ Sharing (UNOS) Liver and Intestinal Organ Transplant Committee, to discuss and begin addressing feedback from the educational forum. Dr. Greenwald explained that no policy proposals are forthcoming regarding this complex issue, which Brian Shepard, CEO of UNOS discussed in more detail during his presentation.

In June, the OPTN approved more detailed standards for the transplant of vascularized composite allografts (VCA) and guidance recommending the transplant community's use of living VCA donations has been published, which Mr. Shepard also discussed.

In anticipation of the implementation date of the Human Immunodeficiency Virus (HIV) Organ Policy Equity (HOPE) Act on November 21, 2013, the OPTN made the policy changes necessary to allow organ procurement organizations (OPO) to perform match runs for HIV-positive, kidney and liver donor recipient pairs. Only HIV-positive candidates who have HIV HOPE Act Institutional Review Board (IRB) approval will appear on those match runs. Dr. Greenwald said that Dr. Jonah Odim from the NIH would cover this topic during his meeting presentation, during which he will provide an update on the status of research criteria being developed by the NIH on behalf of the Secretary of the Department of Health and Human Services.

HRSA also has two OPTN projects under contract. The first one is designed to improve OPO performance data collection; the second project involves the development of a new model for evaluating transplant center performance. Both of these projects have been initiated because of the need for approved metrics and better alignment of the work conducted between OPOs and the transplant centers. John Rosendale and Henri Haskell from UNOS delivered presentations on these projects.

Dr. Greenwald delivered a brief update on the TransNet project, an electronic system launched in 2012 to introduce the labeling and tracking of organs during procurement and transplantation as a way of reducing the risk of errors associated with use of the current handwritten labeling system. David Cartier from the HHS Entrepreneurs–in-Residence Program led this project, which is now being spearheaded by OPTN. There are two applications—one for OPOs and another for OPTN comprising the TransNet system. A draft policy to require that OPOs use the system is being considered. The transplant centers application is being developed and some centers are participating in system testing.

Dr. Greenwald went on to discuss the Scientific Registry of Transplant Recipients (SRTR). She explained that since the last ACOT meeting in March the SRTR contract has been awarded through 2020, and is being administered by the Chronic Disease Research Group of the Minneapolis Research Foundation. The

SRTR is designed to provide statistical and analytical support to the OPTN for use in formulating organ allocation policy, conducting research on organ transplantation, and providing analytical support to this committee.

In addition, a new feasibility study is being initiated through the current SRTR contract on the development of a living donor registry, which Bertram Kasiske, M.D., from the SRTR covered in his presentation.

Informational Update – HHS Innovator-in-Residence Program

Anjelika Deogirikar, R.N., M.S.H.A., CMQ/OE, HHS

Ms. Deogirikar delivered an update on the Innovator-in-Residence Program, which was launched by ORGANIZE and HHS's IDEA Lab. HHS created the Innovator-in-Residence Program in 2012 in partnership with private, nonprofit organizations to promote innovation in health and health care. Ms. Deogirikar explained that she will spend two years collaborating with DoT teams across HHS and with stakeholders across the donation and transplantation ecosystem to find the best governmental and policy opportunities to increase the number of lives saved through organ donation and transplantation. She is working specifically on identifying ways to increase the number of successful and beneficial transplants in the United States. The first phase of the project involves developing an in-depth understanding of the donation and transplantation ecosystem. To achieve this, she has been conducting a listening tour involving discussions with donation and transplantation professionals, recipients, donor families, and living donors to identify the bottlenecks and potential opportunities to increase organ donation and transplantation.

Ms. Deogirikar is now working to refine the potential projects while identifying which ongoing activities can be built upon and defining what could be new opportunities. She is also working to develop metrics that will be used to measure the effects of those projects and is available to attend a future ACOT meeting to share next steps.

Dr. Barr mentioned that Ms. Deogirikar will be interacting with DoT working groups, and he invited questions.

Discussion

Dr. Gerber asked whether the Innovator-in-Residence Program has worked on previous projects. Ms. Deogirikar explained that she is the fourth Innovator in Residence and that several projects have already been conducted, including an examination of aging issues with West Health and a current project with the Healthcare Information and Management Systems Society on patient matching. She noted that HHS has also hired another Innovator in Residence to study aging issues in partnership with the Centers for Medicare & Medicaid Services (CMS).

OPTN Update

Brian Shepard, CEO, UNOS

Mr. Shepard said that the board adopted a new strategic plan for the OPTN for the next three years that changed the 2015 goals on the strategic plan slightly from those that had been identified in 2012. The first change is to the second goal "to improve equity in access to transplants." The change is to clarify that that the second goal is an *equity* goal. Some people were interpreting it to mean that increasing the number would give more people access. This is true but if that were the *intent* of the goal then it would constitute the first goal, not the second one.

Mr. Shepard said that the second, more substantial change in the new strategic planning goals is that, if living donation is really treated as part and parcel of all of the network's goals, the number of transplants, fairness of access, outcome, safety, efficiency—these are all things that would be applied to living donations as well as to the deceased donations. It was appropriate at a point in UNOS's history to pull that out and pay focused attention because it had been an underserved area. Much has been done in recent years to develop new living donation policies. Close attention will continue to be paid to the living donation, which needs to be reintegrated into all the activities of the OPTN. This is why the board made that change.

Mr. Shepard pointed out that, in any case, the goals for the OPTN really have remained similar for the past 30 years for all the strategic plans that have been adopted. What is important isn't just to list five things that UNOS would like to do and let everybody carry on as they were but to actually focus the work of the committee, board, and staff to ensure that the most attention is being given to where change is needed the most.

Feedback exercises were conducted to discuss these goals' relative importance but the focus was not on their moral importance or which are most deserving. Rather, the focus is on where during the next three years to apply resources to move the needle on these five goals (these were the goals from the 2012 plan; the 2015 goals hadn't yet been written). Toward this end, members of the Donation Transplant Community, Board of Directors, and committee chairs and vice chairs have been surveyed. The feedback received was basically the same; that outcomes and safety are important, and much strategy has been formulated in those areas over the past few years, but the number of transplants needs to increase. That number has remained flat, and it's clear that the community believes that what UNOS should be focused on right now is increasing transplants. The board has set a benchmark for allocating resources that support this goal. This is new for UNOS—the decision to focus on some goals to a greater extent than others and to make increasing transplants the top priority. He stressed, however, that this is an aspirational goal, not a budget.

He also stressed that a project will not be cut off over a benchmark. The board will, however, monitor committee work to ensure that efforts are aligned toward increasing the number of transplants. Most of the projects UNOS was working on in 2014 have been completed, but those that don't support this goal have been put on hold. All committees have been asked to examine their resource allocation and work together to increase the number of transplants.

Coincidentally, the number of transplants increased by about 5.5 percent for transplants in October 2015 from the same period in 2014, which comes to almost 1,400 transplants from both deceased and living donors, but numbers for both are also up. Deceased donations are up 6 percent, and living donations are up 3 percent. That's the first time in a few years that the percentage of living donation has gone up. Mr.

Shepard said that this is exciting news, but it's also important to understand why that happened and what can be done to keep that trend going.

He next discussed the KAS, which has been operating for about a year. The system is designed to make better use of kidneys, increase transplant opportunities for some very difficult to match patients, and to prevent disparities in access. The number of kidney transplants has risen slightly even though the number of discards has also risen. KAS data are on the OPTN website, and monthly kidney allocation data reports have been published to help answer existing questions, allow people to ask more, dispel wild rumors, and assist in checking the system. Questions on the system can be directed to him or to Darren Stewart in the UNOS Research Department. He supplied the slides and is well versed on this topic.

In terms of transplant allocation, an increasing number of transplants are going to a slightly younger group of candidates—age 18 to 49—as opposed to those aged 50 and above; however, the older group still represents more than half of the recipients. The number of candidates with high Calculated Panel Reactive Antibody (CPRA) levels who are getting transplanted rose dramatically which, of course, was one of the primary goals of the new KAS system. It has started to drift back down, which was expected to some extent. A large number of highly sensitized candidates remain on the waitlist. It's not clear exactly how long this downward drift will continue, even among the 99 percenters, some of whom are harder to transplant than others. The number of candidates with high CPRA levels is not expected to fall all the way to zero, but it's being watched very closely.

Along with the number of highly sensitized candidates who are being transplanted, a large number of candidates have been waiting five to even 10 years or more for transplants; the number of those who are getting transplants is up fairly dramatically. There is a shift toward African-Americans receiving kidney transplants under the new system and a slight increase in Hispanic candidates with a corresponding decrease in white candidates.

Mr. Shepard also noted that there has been some progress in one of the system's goals: a reduction in the number of recipients who are placed back on the list for re-transplants because they outlived their first kidney grafts. The system does appear to be making some progress in that. Mr. Shepard noted that an examination of the Kidney Donor Profile Index (KDPI) shows that a larger share of very low KDPI kidneys—which are those predicted to last the longest post-transplant—are being transplanted in younger candidates with fewer older recipients than had previously been the case. The recipients of these kidneys should be able to really use the full potential of those kidneys, reducing the number of patients who return to the waitlist, which ultimately benefits everybody on the list.

Mr. Shepard noted that attempts to provide kidneys to highly sensitized candidates, and those who have been waitlisted for long periods often involves transporting them away from the local area in which they were obtained. Logistical challenges have arisen in connection with shipping kidneys to some areas for the first time. For example, differing practices, such as what samples are shipped and when, can trigger confusion. He noted, however, that two-thirds of kidneys are still distributed locally. There has not been a major shift toward one region giving up large numbers of kidneys to other regions.

Mr. Shepard noted that the downside of transporting kidneys for highly sensitized recipients is that cold times have increased and there's been a corresponding increase in delayed graft function. These trends have the potential to undermine some of the benefits of finding kidneys for these recipients and the Kidney Committee is monitoring this. He also noted a slight rise in the number of A2 and A2B and the Bs.

Mr. Shepard noted that a significant spike in the number of discards has also been recorded, particularly involving KDPI kidneys, but this is not due to OPOs over-recovering kidneys that would not have been transplanted in the past. The quality of the recovered kidneys has not changed, and it is not clear why the number of discards has risen; this rate has dropped over the past few months. The Kidney Committee is watching this aspect of kidney transplants quite closely.

Mr. Shepard concluded that the first six months or so of data appear to show that the KAS is meeting its primary goals.

Mr. Shepard turned next to a discussion of VCA transplant programs of which UNOS has 51 approved programs in 23 different hospitals. He noted, however, that the numbers that appear in his slide could overstate the apparent level of activity because all candidates are listed and some transplants were conducted before the regulation took effect last July. A total of 20 candidates are listed and nine have been transplanted since the OPTN took this over about 15 months ago. UNOS hopes to conduct voluntary data collection from some of those transplants. To date, all VCA donors are male, most are white, and they are of varying ages.

Mr. Shepard noted that the recovery of VCA grafts does not appear to be impeding the recovery of other organs from these donors.

Moving on to liver redistribution, Mr. Shepard referred to a slide showing that a candidate's geographical location has a significant influence on whether a candidate will get a liver within 90 days. The variability in probability can vary from 20 percent to 30 percent in some Donation Service Areas to 80 percent in others**,** a fact that the UNOS board has deemed intolerable.

Mr. Shepard reported that UNOS will not be ready to issue a formal policy proposal on liver donations at the spring ACOT meeting but is conducting a transparent and inclusive exploratory process involving two town hall meetings and the drafting of a concept document. The committee is collecting more data and asking the SRTR for modelling based on issues raised at the second town hall meeting

Mr. Shepard then discussed the OPTN/UNOS Membership and Professional Standards Committee (MPSC) outcomes workgroup, which is examining a call to apply an alternate standard for high KDPI outcomes in view of the perhaps widespread assumption that OPOs may be flagged for using high KDPI kidneys. However, this is not the case. The SRTR conducts a good risk adjustment, and programs will not be flagged for accepting them. This topic will be discussed in a public comment period during the spring meeting to elicit general feedback, but no formal proposal will be offered at that time. A different threshold for this type of donation is being worked on, and that will be discussed in general at the spring meeting.

He also mentioned that a new webinar series is being made available that reflect a composite of real-life events that are intended to convey lessons learned. These are safety webinars that roll several events together, but the events are not specifically identified.

Discussion

Dr. Barr asked Mr. Shepard to share any lessons learned from the KAS and the share rules with livers. Is the OPTN working with CMS to determine the impact these changes may have had on the expense to the system either in terms of CMS charges or other third-party payer charges? For example, if more kidneys are being shared over a broader area, as evinced by the increased cold ischemic time, does this result in more pumping of kidneys versus just cold storage or are traveling expenses being submitted in centers'

medical cost reports? He asked whether OPTN and CMS are consulting behind the scenes on some of the charge data.

Mr. Shepard doesn't know of discussion regarding kidney transportation but believes it is warranted because more kidneys are being transported to recipients who need them. The liver committee created a costs subcommittee that worked not with CMS but with OPOs that could incur additional costs and will pass it along; there will also be operational impact. The subcommittee is examining these effects, including potential cost increases, to determine what the impact is likely to be so that the community can weigh them against the potential benefits.

Dr. Barr said that some of these changes will require appropriations.

Dr. Barr also noted that UNOS tracks—and SRTR analyzes—one-year outcomes for high CPRA patients. He asked if KAS could be used to examine the three-year outcomes for these patients as well.

Mr. Shepard said that the KAS will examine this but questioned whether measurement should extend beyond "handy" outcomes to include longer term outcomes that involve measurement of different outcomes at different points. For example, when following the outcomes of transplants involving a small number of people, one rare event can dramatically affect a program's general performance statistics. Perhaps other factors should be examined to determine whether a transplant program is safe even if outcomes vary from year to year.

Stephen Pastan asked whether geographic issues that affect kidney transplants are being examined and, if so, the status of this inquiry.

Mr. Shepard said that both the kidney and liver committees are studying this issue and will address it after establishing a firmer baseline of the current version of the KAS. This will enable them to know what they'll be comparing any changes against and allow them to discuss what questions to answer and what goals to set.

David Gerber asked if rolling data are available on the "Share of 35" now that eight months of KAS data are available. What is the impact of what it has done with organs moving locally and regionally; what is the utilization impact on mortality?

Mr. Shepard said that the liver committee is examining lessons from the Share of 35 in connection with any new liver proposal, and there is data on this issue that he can provide offline.

OPTN Contract Modifications

John Rosendale, UNOS and Henri Haskell, UNOS

Mr. Rosendale

Mr. Rosendale said that the Association of Organ Procurement Organizations (AOPO) has worked over the past year and a half to improve existing donor conversion metrics. This resulted in contract modifications and a study he is leading to examine the feasibility of the OPTN collecting in-hospital ventilated referral data, which the group has identified as the foundation for that conversion metric. The study period will run from October 2015 through September 2016.

The project will be based on five basic research study questions:

1. How feasible is it to standardize the definitions needed to collect in-hospital ventilated deaths across all 58 OPOs?
2. What is the availability of the patient level data across all 58 OPOs?
3. What is the level of effort required to collect these data by the OPOs and the OPTN?
4. How verifiable and auditable are the data submitted by the OPOs?
5. What types of data collection tools could be developed to efficiently facilitate the collection of the data?

Mr. Rosendale said that the philosophy of the project is to look toward the optimal while identifying and working with the current reality. In other words, consider what data should be collected to plan for the long term while moving forward on what can be done quickly and consistently across all organizations. Because this is a feasibility study, some limits may be pushed to determine what is and is not feasible.

The Task 17 Think Tank was established, and it consists of a group of experts to provide ideas and advice to inform task-oriented decision making. The experts were chosen from the OPO pins group as well as the Data Advisory Committee, OPO, and an MPSC subgroup, working on OPO metrics along with John Schneider and other people from the SRTR who did a lot of the work in the last year and a half with the OPO. Collectively, they represent nine of UNOS 11 regions and started the project with their first call on November 17. The goal of Task 17 is to improve OPO performance data collection. OPTN will conduct a data validation study in a sample of OPOs, and it shall include the development and testing of a data collection tool to identify and collect standardized data on how OPOs manage donor referrals.

Mr. Rosendale explained that the project involves examining previous data from work done by the SRTR and AOPO group to establish and refine definitions to determine what the group is working toward and the availability of data among the 58 OPOs. An exhaustive search is also being conducted of all external data sources; both data that is available to researchers and identified and de-identified data to see whether it was de-identified at the source or at what point it was obtained. The purpose is to attempt to obtain a governmental agency agreement that will allow the acquisition of data that researchers cannot usually obtain. The group also hopes to work with donor hospitals over the long term to see whether getting data that is closer to the source will be an option. Then the group will conduct data collection with volunteer pilot OPOs, followed by nationwide, continuous data collection, which will help to further refine definitions.

In addition, the group will explore data collection methods, both from the OPOs and possibly from the donor hospitals. They have begun talking with some donor hospitals systems to see what could potentially work with along with one of the major triage organizations that take calls for OPOs.

The group will assess the burden of the data collection on the OPOs the OPTN, and the donor hospitals, if they are involved. The purpose of doing so is to assess not just what it takes to submit the data but the impact on the work that the OPOs do to get information that is not currently being obtained to see whether it will be disruptive or impose an undue burden on these organizations.

The group also wants to determine whether the data collected could be validated or audited, and they will work with those external data sources and with site surveyors at UNOS to determine this.

The findings will be reported to HRSA along with recommendations and an exhaustive list of what was found throughout the project.

Ms. Haskell

Ms. Haskell shared some of the new work that the new UNOS Member Quality Department has been asked to participate in as part of Task 18, which focuses on transplant hospitals and the potential of developing an alternative monitoring process within a collaborative framework of performance improvement. Under Task 18, the OPTN will conduct a pilot project, led by a quality expert with national standing, to develop and test an alternative model to monitor quality and measure transplant centers' performance. The goal is to improve utilization of hard-to-place organs and reduce organ discards, without significantly worsening outcomes.

She explained that she has been with UNOS for five months; she has been an advanced practice nurse for the past 10 to 15 years during which she conducted extensive quality and performance improvement work.

Task 18 is designed for first year only to reduce the risk avoidance behaviors that are associated with the current monitoring system. As Mr. Shepard mentioned, there is concern that the current monitoring process could penalize people who are innovative or are willing to take high risk organs but she agreed with him that the data does not support that assumption. The current model adjusts for risk, but this pilot project should help to reduce that concern as focus is directed to some of the behavior changes that need to occur.

While developing the pilot, this department wants to allow the participants to be waived from current performance flagging, which will pave the way for innovation and improvement in innovative through participation in this project. Ms. Haskell said that her group held a meeting with CMS the day before this meeting, involving Thomas Hamilton and Dan Schwartz from the CMS team, during which Ms. Haskell's department provided an overview of the project specifics and discussed the project design.

She said there is an opportunity to provide a more concurrent data collection process that will drive improvement, but more real time information is needed to both work toward improvement and provide actionable data. The team also hopes to foster a collaborative approach toward performance improvement. Through this project's design, the group hopes to solicit voluntary participation from transplant organizations that want to work with others and share best practices, share their key learning, and talk about what it takes to improve. This collaborative approach is certainly evident in large scale improvement efforts that other improvement organizations, such as the Institute for Healthcare Improvement, have been able to drive. That is the model that the UNOS Member Quality Department is trying to achieve with this pilot project, which has as its overall aim to increase transplantation.

This first year of the project, which started in October, is the design phase. In the first year, the group is very focused on identifying the process for improvement—what a deployable change management toolkit's elements should be. The next question is what the elements for inclusion will be if transplant hospitals are invited. During year two, the OPTN will launch the pilot project with the participating organizations using a very focused approach and methodology to achieve improvement and innovation. The third year will be devoted to evaluating the project for its effectiveness and its success. To that end, UNOS has contracted with a nationally recognized performance partner, the University Research Company, which has significant experience and global performance improvement work that includes women's health issues as well as HIV in other countries. This firm will help develop that framework for improvement and the changed management toolkit as well as work in partnership with the department and other participating improvement organizations and stakeholders in the community. They will facilitate the design of deployment and the evaluation of the project.

Ms. Haskell's group wants to develop a 10-12 member advisory council, which will include those who have been a part of MPSC—perhaps alumni who are experienced in the work of the OPTN. The goal is to draw subject matter expertise from the community as well as other key stakeholders into this project to include HRSA, CMS, and third-party participation.

This advisory council would be charged with providing guidance to the project along with the subject matter expertise and would be expected to champion and support the project through the life cycle. It's been proposed that the advisory council would meet every two months with the first meeting tentatively planned for January 2016.

The Member Quality Department also has an obligation to continue to communicate to a stakeholder group, which would include representatives from the various transplant societies such as the American Society of Transplantation (AST), the American Society of Transplant Surgeons (ASTS), and the Association of Organ Procurement Organizations. The department seeks to provide ongoing updates to this stakeholder group on a quarterly basis.

Ms. Haskell stressed the importance, especially in the project's design year, of developing relevant participation criteria for organizations that will be involved, such as whether they have the capabilities and capacity to participate in an improvement endeavor to ensure that they are positioned for success.

This effort will also hinge on developing an effective communication plan that will encompass ongoing meetings with the advisory council and the stakeholder group, to MPSC through a quarterly subcommittee, and to HRSA and CMS in a weekly and monthly forum.

With regard to data, the department wants to develop a balanced scorecard to ensure that a proper balance of outcomes in terms of performance, process, care coordination, and some structural measures are examined that will improve the department's understanding of organizations' quality and performance improvement.

This requires the availability of current data, which the department will partner with SRTR to obtain. More current and primarily discreet data is already available, although a component of process measures may require some additional submissions from participating transplant hospitals.

Ms. Haskell also mentioned that collaborative site visits and site assessments will be conducted during the project's first year to learn from participating organizations about specific areas for improvement.

Key steps that will be taken over the next two months will be to recruit advisory council members and develop a formalized recruitment of voluntary members. An open call for recruitment will probably be issued in the summer of 2016.

Discussion

Dr. McDiarmid asked that special attention be focused on the pediatric program. She said that center performance result questions have dogged these programs from their inception because each center deals with a relatively small number of patients. As a result, just one problem can cause outcomes numbers to suffer, which can draw scrutiny from MPSC. She asked that the pediatric programs' special circumstances be considered when center performance is assessed, that this be taken into account during the project, and that someone who represents the pediatric perspective be added to the team that is conducting the project to ensure that these programs are addressed responsibly.

Ms. Haskell indicated that she had noted this request and will take it back to her team.

CMS/OPTN Harmonization

Daniel Schwartz, M.D., CMS

Dr. Schwartz, chief medical officer for the Survey and Certification Group in CMS, said he would present updates and Chris McLaughlin, chief of the Organ Transplantation Branch, DoT, would be invited to comment as well.

Dr. Schwartz said that he would discuss primarily how CMS and HRSA are working together. Some topics relate to the ACOT Recommendation 55 and others concern ongoing communication and collaboration the two organizations conduct regularly. He first listed the names of those on the team who work with HRSA and the transplant community on a variety of transplant issues. All four members of CMS's transplant team are nurse consultants who acquired clinical experience in transplant programs before joining CMS. The team consists of Danielle Miller, Michele Walton, Valerie Caldwell Johnson, and Ekta Brahmbhatt. Sherry Clark conducts much of the communication with transplant programs and OPO organizations and participates in policy discussions. He also mentioned a new team member, Paula DiStabile, a clinical nurse practitioner who has a law degree and a long history and interest in patient safety. Mr. Hamilton is the director of CMS's Survey and Certification Group.

Dr. Schwartz then asked Mr. McLaughlin to describe how CMS has been communicating with HRSA about the TransNet project and with UNOS and OPTN and about how CMS can provide support.

Mr. McLaughlin said that the Medicare programs Conditions of Participation and OPTN's policies require a verification process for organs received and confirmation of blood type between the donor and the recipient. The TransNet system has been designed with the intent to meet both the CMS and OPTN requirements to ensure that no additional regulatory or policy changes are needed. To achieve this, the OPTN has been working with CMS to identify and consider providing specific information regarding the use of TransNet in accordance with CMS's interpretive guidance and, when the timing is appropriate, for TransNet development.

Dr. Schwartz moved on to the next topic: the OPTN's new definition of eligible death does not match CMS's. A change to the CMS definition has not been implemented because if the definition is not achievable over the next month or so, the OPTN will have to decide whether to move forward unilaterally or wait for a CMS regulatory change to ensure the definitions match.

Dr. Schwartz reported that another wording discrepancy issue between CMS and OPOs concerns documentation that needs to accompany organs that go from the OPO to the transplant program. The current CMS interpretation is that this documentation must be kept in written form, but work is underway to determine whether this information can be provided electronically.

Dr. Schwartz also mentioned that CMS has invited its regulatory writing team, the Clinical Standards Group, to most of the meetings that occur between HRSA and CMS. Diane Corning, who is ex-officio member to ACOT from CMS, participates and is well aware of some of the issues and the work that needs to be done to ensure that CMS regulations don't impede the OPTN in doing some key work.

Dr. Schwartz then introduced the topic of OPTN stand-alone living donor surveys. He recalled that, after ACOT 55, a crosswalk was conducted to identify overlap in OPTN policies and CMS regulatory

language. The living donor survey was among the few overlaps that were found, and work is underway behind the scenes to determine what can be done to decrease the survey burden. He invited Mr. McLaughlin to comment. Mr. McLaughlin reminded meeting attendees that OPTN is moving toward combining the living donor survey and transplant program surveys and plans to have the majority of these combined by January 2016. Dr. Schwartz mentioned that efforts are also underway to limit the number of visits OPTN and CMS make to transplant program sites.

He then went on to talk briefly about organ-specific innovations that improve transplant outcomes, which CMS does not want to stifle. For example, about a year ago, the agency changed the regulation language on mitigating factors to specifically indicate that innovation would be considered if a program has trouble meeting the outcomes regulation in the Conditions of Participation. Thus, programs should alert CMS of innovative practices that they want to pursue. The agency looks favorably on innovative practices and is discussing such practices with Mr. McLaughlin, his team and HRSA before making a definitive decision to ensure that the new practice conforms to OPTN or UNOS policies, bylaws and procedures and, thereby, that those practices will be supported by HRSA. CMS welcomes innovative practices, hopes more will be forthcoming, and intends to be very supportive of such practices or pilot projects as they emerge. Mr. McLaughlin added that DoT is happy to review anything and is open to reviewing such new approaches.

Dr. Schwartz moved on to a discussion of a new OPTN quality assessment and performance improvement (QAPI) policy. He explained that CMS believes having a functioning and effective QAPI program is the key to maintaining and improving quality and performance and is pleased to see the new OPTN policy, which is not a burden or an unnecessary overlap because Medicare Conditions of Participation require programs to have a QAPI program.

CMS collaborated with AST and ASTS to produce a series of 12 webinars that describe in detail what a functioning and effective QAPI would look like to a CMS survey team, and the agency's specialized QAPI surveyors are presenting this material in the webinars, which are in the 9th or 10th of this monthly series. The webinars have been archived, and Dr. Schwartz believes they are available on the AST and ASTS website for anyone to review.

Mr. McLaughlin confirmed that an OPTN bylaw that requires transplant centers and OPOs to have QAPI programs was in effect as of September 1 of this year. OPTN believes this bylaw should be and is consistent with CMS's requirement. The OPTN QAPI requirement will not be routinely monitored by the OPTN contractor through site surveys or other means, but the OPTN may always request information about a QAPI program and is likely to do so when it has serious concerns about performance.

Dr. Schwartz then delivered several outcome measure updates. He said that CMS is interested in the Bayesian methodology that the OPTN and SRTR are using and has found that the resulting outcomes do not differ much from the methodology that CMS is using. The agency will probably conduct another comparison of the two methodologies after the next SRTR outcomes report is released. The agency is not contemplating regulatory changes in this area. However, it plans to keep an eye on the Bayesian methodology to ensure it is usable in the long run, and the thresholds remain stable.

He said that, on the OPO side, CMS is aware of AOPO's proposal for a new OPO performance metric and has had conversations with HRSA about the proposal and the OPTN efforts on data collection analysis that would support metric changes. The agency is still examining this but is pleased to see some proposals for potential outcome measures from the community. They will work closely with HRSA or any organizations as new ideas are put forward to determine what works best for all in examining outcome measures in the future.

Donor Management Research and Innovation

David Gerber, M.D., ACOT

Dr. Gerber said that there is a limit on the number of quality organs for transplant and an increase in donor after cardiac death and marginal and expanded criteria donors. Donor quality is defined by post-transplant outcomes according to risk of graft loss (patient death or need for re-transplantation). Inferior organ quality engenders recipient morbidity and mortality. There is a need to mitigate recipient waiting list morbidity and mortality.

There are also obstacles to research and innovation in deceased (brain-dead) donors.

There are a number of constituents, including scientific investigators, donors, families, hospitals, logistical OPOs, OPTN, and regulatory issues (waiting list candidates and transplant recipients/centers).

The current infrastructure is inadequate to support effective donor intervention and treatment studies. The magnitude and complexity of the challenges require guidelines and processes to facilitate the optimal design and safe execution of clinical trials in deceased donors.

A secondary challenge is doing research among the deceased population.

It is also important to consider risk to the community; with a single-organ transplant, would another transplanted organ be affected?

There are three basic groupings: donor-focused issues workgroup (responsible for obtaining donor authorization for clinical research), donor-side review, and approval of research and donor-family communications. The oversight workgroup conducts national review, access to protocol, uniform study approval process and adequacy of monitoring, and the transplant-center issues workgroup, which is responsible for obtaining recipient consent, levels of risk, knowledge about research protocol, and implications for acceptance and allocation.

Dealing with recipient consent and levels of risk, the question arises of how to communicate knowledge about research protocols so that recipients can understand the implications for acceptance and allocation. Once the attempt is made to expand the number of high-quality organs for transplant, what is the decision-making level for organizations and recipients about allocation and acceptance? How do you mitigate the impact of research protocols for patients?

Focus guidance on big science. For people doing donor-related research in small trials, it’s important to identify policies and guidance that would expand the pool of higher quality organs. All donor activities need to be identified.

Representatives from several of the large major transplant societies—AST and ASTS—went to the Institute of Medicine (IOM) to ask the institute whether it would review the issue of donor-related research as it has some other large population-based research activities and provide guidance where it could. Representatives of those transplant organizations and key stakeholders met with the IOM last July. After reviewing the details of where the challenges are from the perspective of those in the transplant field, the IOM is looking at putting together a study that would be complementary to ongoing activities.

The work group tried to develop, complementary to what happened with the donor management and resource meetings that were being held, a sort of timeline of what the different areas of challenge would be. Looking at this from the research perspective, obviously the first level is developing a proposal with multiple levels of input to develop a study plan and have that get communicated in sort of a research consortium way. The group discussed such things as where the challenges would be and how to get this information to the OPOs.

Donor-related research could create an increased pattern of work and a change of practice for OPOs. Some level of scientific merit review must be applied consistently across these studies and there is a level of human subjects review. What's unique about this is that subjects aren't the donors but the recipients of the organs provided by donors who were in the research study.

Trying to determine levels of risk is important in being able to further educate potential transplant recipients. The level of risk of a study as perceived by a transplant center and/or their patients could have an impact on the allocation of the organs. It is also necessary to have a level of transparency and data monitoring and the ability to communicate that across the spectrum. Akin to the conversation that Mr. Shepard said he had earlier, what was observed with the KAS was a sudden rise in the number of nationally transplanted kidneys, by about 17 percent. And nearly one in five recipients at a national level is getting an organ from somebody who was involved in a donor-related study, and that wouldn't necessarily be in the OPO where the study was being done. The transplant recipient could be elsewhere in the country.

The staff committee has met many times over a year and a half or two years and received lot of input from ACOT, including people on this work group and outside organizations. These include staff from HRSA, UNOS, transplant clinicians who are involved in donor research, and members from the OPO community.

It is also important to identify what role ACOT could or would play in this. The committee broke this down into the topics that needed to be addressed. These range from donor-focused issues, standards that the OPOs would be able to review, and how they would be able to participate in this process and understanding the work that a donor hospital considerations would be. Another consideration is how that would impact the relationships between OPOs and their donor hospitals.

The transplant-focused issues include quantifying the potential risk of these donor-based studies and communicating the information about the protocols to the accepting team in a transparent way. It's important to ensure that this information is put out there so that those centers and their potential recipients will be able to obtain or opt out of receiving organs from these donors. There is also the issue of informed consent for those recipients and ensuring there is a way to document informed consent. These were all topics that have been addressed in various sub-committee meetings.

The staff committee has developed a recommendation that ACOT is invited to vote on at this meeting. Dr. Gerber offered to read the recommendation, which has been distributed to everyone at HRSA and the Office of the General Counsel. It appears below. Available ACOT voting members were asked to vote. The recommendation contained a seven-point preamble and the recommendation:

DRAFT ACOT Recommendation

WHEREAS, the Committee finds that:

1. Clinical innovation through deceased donor intervention research (DIR) has the potential to substantially increase both the quantity and quality of organs to mitigate the increasing gap

between the number of available organs (supply) and the number of patients with end-stage organ failure waiting for transplantation (demand);
2. DIR creates multiple considerations for transplant candidates on the waiting list (e.g., risks of potential adverse impact on organ quality, function, and outcomes; adequate understanding of such risks in order to provide appropriate informed consent to accept such organs; and the timing and logistics of presenting the necessary information to candidates about the specific nature of the research interventions);
3. A variety of ethical (the specific transplant recipient is typically not known in advance of the research intervention) and regulatory (scope of OPTN oversight of potential safety risk of DIR) barriers and challenges has stifled clinical innovation and progress;
4. Conducting DIR impacts the donation and organ procurement process at the deceased donor level involving all 58 OPOs, thousands of donor hospitals nationwide, and at the transplant recipient level involving thousands of transplant candidates and recipients at hundreds of transplant centers nationwide;
5. A broad based consensus of the organ donation and transplant community has concluded that only a mandatory national centralized oversight of DIR with a single consistent review process operated within the auspices of an independent entity with access to the necessary specialized expertise, such as HHS and preferably independent of the OPTN, can effectively address the complex barriers and facilitate DIR. This will assure reasonable protections for potential and actual transplant recipients of such organs, gain broad support within the organ donation and transplant community, and maintain the public trust in the integrity of the organ donation and transplant process;
6. The IOM completed a planning meeting on July 14, 2015, with respect to undertaking a study on issues in DIR, and has begun to obtain commitment of funds to proceed with conducting this study. Completion of this study should not delay actions by the Secretary to act on the following recommendation;
7. Efforts are already underway by multiple agencies and organizations (CMS, HRSA, OPTN, and SRTR) to evaluate and implement mechanisms for risk-adjusting outcome measures and center-specific reports that would reduce barriers for broader participation in donor intervention research, thus potentially increasing both the quantity and quality of organs available for transplantation.

The Committee RECOMMENDS that the Secretary:
1. Take timely action to establish the framework for a mandatory nationwide centralized oversight mechanism within HHS to facilitate deceased donor (and organ) intervention research by any entities conducting such research and begin the preliminary process to complete such mechanism without waiting for completion of the anticipated IOM study; and
2. Support financially and facilitate the planned study by the IOM on issues and challenges presented by deceased organ donor clinical research, and incorporate such findings of this study into the framework established in part (1) above.

A question was raised: If the IOM doesn't go ahead with the study because it doesn't raise money will that affect the recommendation at all?

Dr. Gerber responded that it does not and that wording was included in the preamble acknowledgement of the IOM. He also thanked Sandy Feng, M.D., Ph.D., from the University of California, San Francisco, who also drove the IOM meeting.

Dr. Feng said up to 70 percent of funds were raised for this effort, and there are multiple avenues of action to try to bring this issue to another plateau over the next couple of years.

Ms. Stroup from the DoT conducted the roll call vote:

Dr. Barr	Yes
Mr. Alexander	Yes
Dr. Becker	Not present
Ms. Caley	Yes
Dr. Coleman	Yes
Dr. Fung	Not present
Dr. Gerber	Yes
Ms. Glazier	Yes
Dr. Hands	Not present
Mr. Lara	Yes
Dr. Matas	Not present
Dr. McDiarmid	Yes
Ms. McDonald	Yes
Dr. Molina:	Yes
Dr. Pastan	Yes
Ms. Puryear	Yes

Ms. Stroup confirmed that a quorum had been obtained, and that all voted yes.

Dr. Barr thanked all present for participating and said that the issue of intervention on the work of the transplant side for recipients, as brought up by both Drs. Matas and Schwartz along with Mr. Hamilton, could be brought up in future meetings.

Advisory Committee on Blood & Tissue Safety & Availability (ACBTSA) Update

James Berger, M.S., M.T., (ASCP) SBB, Executive Secretary, ACBTSA

Dr. Berger explained that the ACBTSA held its 47th meeting on blood and tissue safety and availability at the Department of Veterans Affairs in Crystal City, Virginia, during the week prior to this meeting. The meeting focused on short-term funding strategies for securing funding for blood safety innovations, and it was divided into four different parts. These parts were the background on the issue, during which the hospitals and the users gave their perspective of where they're seeing the blood safety innovations being affected; the budget impact from a purchaser's and payer's perspective; committee updates; and an update on the tissue products and emergency preparedness symposium on which Tim Pruitt provided an update. The FDA's Blood Products Advisory Committee meeting provided an update. The Blood Systems Sustainability Subcommittee also provided an update.

The committee's findings were that maintaining an adequate supply of safe blood for transfusion is integral to public health and a national priority. Illustrations of that fact are that 10 percent of hospital-based procedures require the use of blood, and that within the Medicare population approximately 17 percent of in-patient claims included blood use.

The next finding was that blood utilization data understate the need to have reserve blood on the shelf prior to conducting many medical and surgical procedures. When considering potential need, data indicates that about 20 percent of hospital procedures require or could require the use of blood.

The third finding was that dramatic reduction in blood use—approximately 25 percent currently, with projections of up to 40 percent by 2020— which has been ongoing since 2008, has created a current crisis of economic instability in blood-banking, which has worsened since the committee first examined the issue in 2013.

The last finding in that group was that the instability in the blood centers threatens to exacerbate existing spot blood shortages, reduce resilience in the face of public health emergencies through elimination of search capacity, and reduce ability to provide the most appropriate routine specific products and services.

The committee recommended that an interim report from the Rand Corporation be presented at the next meeting of the ACBTSA. Rand was recently contracted by the Office of the Assistant Secretary for Health to examine the sustainability of the blood system to see what could be done in the future to improve it, whether it's sustainable and, if not, make recommendations.

The next recommendation was to facilitate a process for blood centers to collaborate and dialogue on innovative strategies to address their new economic realities. An example of that would be the anti-trust safe harbor. Dr. Berger explained that anti-trust laws prohibit these blood centers from discussing safety issues.

Another recommendation was to provide advocacy to CMS and Congress on measures that could be taken to address the gap in reimbursement of blood components as a special need in the public health system. This could include a carve-out; in other words, a direct pass-through, enabling CMS reimbursement of blood centers for the actual cost of the blood components, including implementation of newer safety innovations based on the special role of transfusion as a public good in supporting modern health care.

One example would be immediate line item additive congressional funding for hospital purchase of blood components.

Another recommendation would be to ensure that studies of the crisis in the blood system address the following issue of whether open competition among blood centers is the optimal model for the U.S. blood supply. To provide perspective: the U.S. has approximately 300 hospitals and about 80 blood centers that collect blood. Canada has just two blood collection systems, and the U.K. and France each have one system as do many others; we have open competition.

The next recommendation is to study adverse effects of an unconstrained competitive environment and blood collection with avoidance of potentially adverse outcomes for public health. For example, that would be monopoly or oligopoly behaviors in the absence of suitable controls.

The next recommendation is the need to preserve search capacity to address public health emergencies.

Another one is the need to maintain resources for research product innovation and implementation of newer measures to assure and advance blood safety, efficacy, and availability.

The last recommendation is the structural cause of the gaps and misalignments between cost and blood production. This would include the cost of maintaining a reserve inventory in excess of predicted need. In other words, there is always a need for surge capacity.

Dr. Berger said that he met with the Office of the Secretary of Health to go over those recommendations and reported that she wants to move forward with them.

In closing, Dr. Berger reminded those present that ACOT has an ex-officio member to this committee, and there is always a chair for ACOT present.

HOPE Act – Update

Jonah Odim, M.B.A., M.D., Ph.D., National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health

Dr. Odim said by law, they met for the first time in the U.S. on HIV-positive to HIV-positive transplants under an IRB-approved research protocol and in compliance with the HOPE Act, as well as the final safeguards and research criteria that await publication momentarily. The only world experience in HIV-to-HIV organ transplantation is from South Africa by Ms. Elmi Muller who presented her excellent results in 27 HIV-to-HIV kidney transplant patients. However, there is really no such evidence for safety efficacy or effectiveness in North America. And in alignment with the mandate of the HOPE Act, the final safeguards and research criteria are really meant to support the acquisition of new clinical knowledge and mechanistic insights about HIV-positive to HIV-positive organ transplantation in the country.

Dr. Odim explained that the law was signed in late 2013 and, following the delegation of authority from the Secretary to NIH, then the re-delegation to NIAID, a small working group was formed that has met continuously since then to draft the safeguards and research criteria with input from stakeholders and transplantation and HIV medicine communities.

After a 60-day public comment period on research criteria, which ended in the fall, 13 public comments were submitted by a combination of individuals, the transplant community, and a municipal HIV agency. Dr. Odim reported that the final safeguards and research criteria should be released shortly; they have already cleared the NIH and are in the Office of the Secretary for final clearance and publication.

The Secretary and the OPTN will review the outcome data and results of the research by November 2017.

Dr. Odim provided an overview of some of the comments that were submitted in response to the published draft research criteria. Some pointed out that HIV-infected donors may be at long-term risk for renal and or liver disease; for example, individuals with particular levels of alpolic lipoprotein 1. As a result, some centers said they would not accept donations from HIV-positive prospective donors.

Another commenter felt it was premature to embark on living HIV-positive donors without collecting information on prior experience with deceased HIV-positive donors. This commenter favored a staged approach to an introduction to this type of research.

Dr. Odim argued that the evidence for the safety of organ donation by an HIV-infected individual will only be generated by clinical research. Voluntary participation in HIV-positive to HIV-positive transplant research must be based on informed consent that involves a description of alternatives, risks, potential benefits, unknowns, and the need for long-term patient follow-up. Such studies should be free of coercion, and the research should be carried out by teams with IRB approval. The discussions should also address how research injuries are managed and paid for in the short and long run. An advocate independent of the research team should also be made available to advise the HIV-positive individual.

The need for independent advocates was also mentioned in several comments. Some strongly supported the requirement for advocates for both the HIV-positive recipient and prospective HIV-positive living donor. Others viewed this as unnecessary and duplicative of the principle investigator's expertise. The working group felt strongly that the advocate should be an additional knowledgeable person who is neither a member of the research team nor the patient's health care provider. This person would provide information, answer questions, and provide assurance of equal access to health care regardless of the patient's decision about whether to participate. For example, the advocate can ensure that the transplant candidate is aware of his/her right to be offered and accept an organ from HIV-negative deceased donor if one should become available. The advocate can also assure the prospective living donor of confidentiality and support if he or she determines that donation is not in his or her own best interest.

The next topic that elicited extensive comment focused on the transplant hospital experience. Several academic institutions, professional societies, and the OPTN indicated that the requirements for physician and surgeon experience in HIV-negative to HIV-positive organ transplants were excessive and would result in few centers being able to participate in the research allowed under The HOPE Act. Dr. Odim said that, in response to this wide consensus on this issue, the group has accepted the AST's and ASTS's suggestion on reliance on the teams rather than on an individual's experience, with the bar set at five cases of HIV-negative to HIV-positive transplant patients over four years, to establish systems and processes involving HIV-infected individuals in the transplant scene, and the issues related to drug-to-drug interactions, which are quite complex.

Other comments focused on donor eligibility criteria in connection with immunologic criteria, (i.e., CD4 T-cell counts and HIV viral loads). Many commenters raised concerns about the usefulness and relevance of requiring a minimal level bar for CD4 and T-cell counts in the donor, arguing that these counts will not predict allograft function, as evidenced by Ms. Muller's experience in South Africa, where many of her transplants had excellent outcomes. Kidneys were donated by many donors who had CD4 T-cell counts

well below the minimum of 200. In response to this comment, although the collection of CD4-positive cell counts during the evaluation period is required, no minimum criteria with regard to the CD4 T-cell level will be imposed for organ acceptance.

Opinions expressed regarding viral loads in the plasma and the risk of transmitting potential drug resistance varied. Some felt that donors with any viral load should not be used, but others disagreed. However, the evaluation window does not make it possible in all cases to mitigate the risk of transmitting viral resistance by vetting viral load limits and/or assessing antiretroviral-resistant profiles among potential donors, although many potential donors' medical history will permit adequate assessment and reduce the risk of virus transmission.

Several commenters emphasized the importance of a pre-transplant organ donor biopsy. The final criteria include a requirement for performance of a pre-implant "back table" biopsy. Although there are no further specimen collection requirements, the working group felt strongly that the inclusion of serial bio-specimens in the individual research protocol should be encouraged. The group feels that these specimens will be a valuable resource in studies related to super infection risks.

Several commenters expressed concerns about data collection quality and reporting. The HOPE Act requires the Secretary to review the results of research conducted under the law. And the purpose of the final safeguards and research criteria was to ensure all investigators conducting research in this HIV-positive to HIV-positive transplant protocol collect similar data element. This standardization-facilitated subsequent review is also mandated in the HOPE Act.

One commenter pointed out that the risk of performing transplants involving HIV-positive-to-HIV-positive transplants is unknown, and they are not included in center-specific reports, which could serve as a strong disincentive for centers to take on these patients leading to fewer patients receiving life-saving organ transplants. This is an important issue, but the group felt it was really beyond the authorities delegated to NIH and NIAID.

In terms of donor eligibility, there is no evidence of invasive opportunistic complications from HIV infection. A pre-implant donor organ biopsy is to be obtained, and there is no viral load requirement. For a deceased donor with a known diagnosis of HIV and all prior anti-retroviral therapy, the study team must describe the anticipated post-transplant retroviral regimen to be prescribed for the recipient and justify its conclusion that the regimen will be safe, tolerable, and effective. This is a very important aspect of the informed consent process.

With regard to HIV-positive living donors for programs and/or donor recipient pairs that choose this option, the criteria are: CD4 T-cell counts above 500 for a six-month period before donation, undetectable viral load, no evidence of invasive opportunistic complications of HIV infection, and, for the living donor, pre-implant donor organ biopsy. The HIV recipient eligibility criteria mirrors essentially the criteria established in the NIH transplantation stock trial of the last 10 years, implemented essentially around the world, including South Africa. The recipient criteria for kidneys is CD4 T-cell count higher than 200. For liver, it's higher than 100 at 16 weeks prior to transplant, no history of opportunistic infection—if there's a history of opportunistic infection, that count gets bumped up to 200—undetectable viral load accompanied by a stable anti-retroviral regimen with no evidence of active opportunistic complications of HIV infection, and no history of primary CNS lymphoma or progressive multifocal leukoencephalopathy.

The other categories in term of criteria include the transplant hospital criteria. The team-experience requirement in HIV-negative to HIV-positive organ transplantation is organ-specific and, as previously

mentioned, essentially five HIV-negative transplants in HIV-positive patients over a four year period. The transplant hospital needs to have an established program of HIV care and HIV program expertise on the transplant team.

OPO responsibilities include the development of standard operating procedures and staff training procedures on working with deceased HIV-positive donors and their families and a bio-hazard plan to prevent and manage HIV exposure and/or transmission. These are minimum measures.

Required outcome measures for the waitlist candidates would include the HIV status, CD4 T-cell counts, co-infection history with hepatitis C, hepatitis B, viral loads, and ART resistance issues, if they are removed from the waitlist, or death for other reason and time on the waitlist. For all donors, whether they are living or deceased, required outcome measures are the HIV status, T-cell counts, viral loads, co-infections, history, and ART resistance. Outcome measures in potential living donors are any progression to renal insufficiency in the kidney donor progression, hepatic liver failure, insufficiency in liver donors, change in anti-retroviral therapy as a result of organ dysfunction, progression to AIDS, failure to suppress viral replication, and death.

Finally, outcome measures for transplant recipients are rejection rates annually for up to five years, progression to AIDS, new opportunistic infections, failure to suppress viral replication, HIV-associated organ failure, malignancy, graft failure, and mismatched ART resistance vs. donor

Dr. Odim said he expected to hear back from the Secretary on these recommendations by the end of this year.

Dr. Pastan asked whether there will be separate funding for centers that wish to conduct this research to support the various extra requirements, such as tissue banking.

Dr. Odim said that the HOPE Act does not mandate funding for this research; researchers will have to seek their own funding sources, but NIH is likely to be a funding source.

Dr. Matas commented that the issue of excluding center-specific results is an important point that does not just apply to this area of research, and that this needs to be a broader topic of conversation.

Dr. Barr agreed and said it would be discussed during the new business portion of the meeting.

Scientific Registry of Transplant Recipients – Living Donor Registry

Bertram Kasiske, M.D.

Dr. Kasiske described the SRTR report and provided a living donor registry update.

Dr. Kasiske pointed out that the first living donor, Ronald Lee Herrick, who made kidney transplantation possible, died of cardiovascular complications while receiving maintenance hemodialysis. This case serves as a reminder that much more is known about donors' short-term complications than about long-term ones. As a result, HRSA put into the SRTR contract proposal a requirement to devise a feasibility study for a living donor registry.

The study's purpose would be to learn how donation affects the donor. Are there populations that are affected differently? This information could be used to better estimate risk and improve informed consent. It may also be used to optimize the donor evaluation and follow up, especially if it identifies high-risk populations.

These questions about long-term follow-up are difficult to answer without very large numbers, because the important events, like death or, in the case of kidneys, returning to dialysis, are rare, and long-term follow-up is needed because these events accrue relatively slowly over time. Another very important feature, and one that has generated controversial literature, is the need for comparable controls, so selecting controls that don't have a selection bias is very important part of this picture. For these reasons, a registry is needed along with, if feasible, identification of control subjects.

A conference was held to address these issues in 2009, and a meeting report was published that contains several germane recommendations.

The report's authors suggested delegating living donor follow-up beyond three months to a third-party organization. The basis for this suggestion was that OPTN data is probably pretty good for reporting perioperative and short-term complications. However, the outside organization could obtain follow-up consent before donation and would include maintenance of contact information on living donors, surveillance for the development of specific comorbidities, serious and rare events, and facilitation of future investigations of donor outcomes.

Another recommendation was to provide additional ascertainment of serious events, such as deaths and end-stage renal disease, through linkages of the OPTN/SRTR database with existing public databases, such as the Social Security Death Master File, the National Death Index, CMS data, and probably other data sources over time. The data could include psychosocial and socioeconomic outcomes, assessment, and mid- and long-term follow-up of living donors.

The proposal in the contract to conduct a feasibility study that could lead to this donor registry would include identification of donors and importantly control cohorts, development of a consent form, frequency of follow-up intervals, and the development of survey instruments and data collection forms to monitor intermediate to long-term development of comorbidity and serious events. Additional benefits would be an assessment of psychosocial and socioeconomic consequences, methods for data collection, and detailed estimates of start-up costs and subsequent annual operating costs. All of this would have to be completed by June 20, 2016.

An ideal registry would include collected data on all living donors in the United States, but it's not clear that these forms would be adequate for collecting data for registering living donors.

Controls would also be necessary with as little bias as possible. This would lead to determining which donor candidates who do not become donors could be ideal controls and on which the same data would be collected in the same way they are collected on living donors. Consent on both the donors and controls would have to be obtained at the initiation of the evaluation process so the data can be collected and linked to other registries. They would have to be willing to take subsequent quality of life surveys, for example.

The best way to register controls—which is a key issue—could be to collect data only when it's determined that donation will not take place due to factors that really cause the least selection bias. For example, if there's an immunological barrier, and the donor who otherwise would be a donor cannot donate, that person can be designated a person, a control, on whom data would be collected, minimizing

the data collection burden on the transplant center. However, the center would have to identify who the controls would be, and this could be an almost insurmountable barrier.

The other option is to collect data on everyone who comes to the center for an evaluation; the only other piece of information that would have to be collected is why potential donors decide not to donate. This step would permit the long-term analysis, not only of those who would otherwise have been good candidates and will end up being good controls, but also those who were turned down from donation to see truly if they had the health outcomes that the center expected, vis-a-vis developing diabetes or cardiovascular complications. This information could inform transplant programs about whether their decisions to turn potential donors away were appropriate. But this step increases the amount of data centers would be asked to collect.

Another key question is whether current data collection forms are adequate. The living donor registration form is quite good; it collects a lot of information on demographics, socioeconomics, transmissible diseases, kidney function, and cardiovascular risk. It does not record some rare events, such as whether somebody had a coronary artery stent inserted a few years before evaluation, but were nevertheless being evaluated for donor suitability.

Whether other data should be collected as part of the registration process and then, what are the long-term outcomes of interest, are also points of discussion. This answer would be driven by outcomes that it's assumed would be important to the patients and to the donors: morbidity, all-cause mortality, end-stage renal disease, cardiovascular events, hospitalizations, health care costs, and quality of life. Some of these data might be obtainable, if not from all donors, from a representative sample over different time intervals. Standardized instruments, such as the SF-36 for example, could be used to get information that is more unique to donors.

Donors have not been asked what they would like to know about their outcomes, and the SRTR hopes to make this part of the feasibility study. Because the issues for kidney and liver are quite different, there is a separate committee for both types of donors. Meetings on this project have already been held.

A pilot survey of donors or individuals who come in for evaluation to be living donors will be conducted to determine how many among those who come in decide not to donate. Eight sites have been recruited to participate in this survey distribution exercise. A process to get expedited IRB reviews at these sites is underway followed by collection over a four-month period of these surveys, which will be brief and will help generate estimates of time, effort, and cost that might be involved in a registry like this.

Brief program-wide surveys will also be conducted to determine their opinions about participating in a registry, with a particular focus on obtaining consent from everyone who comes in for an evaluation. Another goal is to complete the living donor registration forms, not only on people who end up donating, but also on those who come in to be evaluated.

The concept of collecting blood for storing for future DNA analysis will also be explored, as well as what's involved in maintenance, and the periodic provision of living donor contact information so that these donors can be followed over time. The results will be tabulated to gauge the level of buy-in participation. Some pilot analysis will also be involved because centers will not be counted on to provide follow-up data. The key here will be to take the cohort and link to other databases. This will be conducted as a demonstration project that links data from living donors to SRTR and CMS data and to the National Death Index. Pharmacy claims might also be a good source of information on who, for example, gets diabetes or hypertension and the feasibility of linking to other databases in the future will also be

explored. Eventually—10 to 20 years from now—there may be an opportunity to link these data to electronic health record systems and other sources to get much more detail on outcomes for these donors.

The group has also considered asking donors and controls to consent to have their blood stored for future DNA analysis. Pilot data on the feasibility of this shows that blood samples are not as difficult to obtain as it may seem. This permission would be helpful in determining whether to assess risk in connection with genetic background, such as the APOLi genotype. Some centers may already be doing this. This would entail identifying a secure site, determining some of the logistics and costs associated with shipping and storing, and then ultimately establishing a committee that would make recommendations of when samples should be analyzed, so that, when a worrisome gene polymorphism is detected, researchers can go back and actually look among donors that have stored samples.

Discussion

Dr. Matas asked what the limitations are of all this linking? Is there selection bias and how do you get around all of that?

Dr. Kasiske said that registering everyone who comes in for evaluation would allow for identification of a control group with minimal selection bias.

Affordable Care Act and Transplantation – Update

Eugene Freund, M.D., M.S.P.H., CAPT, USPHS, CMS

Dr. Barr introduced Dr. Freund, medical officer at CMS. Dr. Freund said he would discuss some of the impacts of the Affordable Care Act (ACA) and hoped to hear from those present about how it is affecting patients' ability to obtain transplants. He noted that the guaranteed issue provisions have made it possible for people with pre-existing conditions to get health insurance to cover transplants, especially in the ACA Marketplace. The ACA has ended arbitrary decisions and lifetime or annual dollar limits, with a few exceptions, such as grandfathered plans, which had probably been an issue.

He said he has heard disappointed reactions from people with end-stage renal disease who have skipped the Marketplace, and purchased a short term policy—defined as a less-than-full-year plan—which doesn't have to meet ACA requirements. These plans can limit what procedures are covered and have lifetime limits as well. But Marketplace or employer-covered policies covering transplants can require prior authorization and drug formularies. He asked to be told about what meeting attendees have been hearing about barriers to care they are hearing about from patients.

Discussion

When asked whether more information about such issues that are being reported will be made public by spring, Dr. Freund said that lists of such problems are not being compiled, but he is made aware of those that occur in the federally facilitated Marketplace and are not resolved. Others may be resolved at the state departments of insurance level, but a distributed complaint system makes it difficult to know whether solid data about the types of problems that are arising will be available. He said his standard advice to those who are encountering problems is to first go to the issuer. Patients have the right to appeal and obtain an independent review of a negative decision. The next step would be to go to state insurance

commissions, to Marketplace hotlines, or to CMS, especially if there are claims involving life threatening conditions that are not being properly resolved.

Mr. Shepard suggested that some problems that Dr. Freund is not hearing about involve state Medicaid plans and cost discrepancies between per diem hospitalization charges and true coverage of expenses.

New Business

Dr. Barr mentioned that the work group that had been presenting on door interventional research is no longer necessary, and a recommendation to this effect has been approved.

He raised an issue that Dr. Odim among others had mentioned regarding program-specific reports and risk adjustment to avoid disincentives to obtaining/transplanting certain types of organs. He asked whether ACOT could be of any assistance here. Mr. Hamilton mentioned that CMS is following SRTR's lead on this.

Dr. Matas said that the SRTR, CMS, or HRSA and private insurance companies need to be involved in this issue. The bottom line is each is acting by their own mandate, but the end result is that centers present results that don't control for a number of variables. This affects center practices. When people are worried about trying innovative approaches or new drugs that might not be effective, this affects centers' willingness to be innovative. It is important to try to develop a common understanding of what patients could or could not be excluded from center-specific results; on that, we need to come to some common ground if such a practice is not overused.

Dr. Kasiske acknowledged that efforts to study this issue have been lagging. The focus has been on risk avoidance, but he stressed that it's important not to "mess with" the statistical models by removing patients and variables that do a good job of adjusting risk, because then the models become unstable and don't work well. He added, however, that the results of those models can be weighted. For example, regulatory groups could weigh results so that higher risk transplants are not as likely to cause a center to be flagged.

Dr. Barr said he was unsure whether it was necessary to establish a work group to bring people together to tackle this issue, especially if efforts are underway by the MPSC, the SRTR and others to develop a solution. He asked attendees to think about this and email him or Ms. Stoup their thoughts to be shared with key people in other organizations to determine what role, if any, ACOT should play.

Dr. Pastan said that the issue of organ discards and shying away from high KDPI organs is an issue as well. The National Kidney Foundation is trying to sponsor a consensus conference on organ discards next fall. He said he would put his thoughts in writing and send them to Dr. Barr.

Public Comment

Ms. Stroup said that two members of the public, Jane Zill and Christine Wright, had submitted letters to be read at this meeting, but neither women were in attendance. Their letters have been entered into the public record.

Another member of the public, Ms. Mary Faith Harty, delivered comments as well, which appear verbatim below.

Ms. Harty:

Yes. My purpose in coming to the ACOT meeting was to appeal to the Secretary. From the past meeting notes I see that you had the Secretary here. From my work in the last two years, trying to get through the system, I have found horrible, horrible errors and mistakes, starting with the UNOS listing, which is also a concern for living donors and HIV-positive usage and the use of programs that appeared to be not policed by UNOS yet still approved. I have come to find that the public, in general, is not being listened to, and our concerns are relegated to surveys and committee meetings, after the fact and in hindsight, and based upon the input of individuals that are within the industry of the Gifts of Life, inclusive to the alliance and without representation, such as an independent council.

This would also be inclusive of a transplant task force that can act in a swift and just manner with full accountability and penalties and fines for those offer egregious errors and are not fulfilling other requirements of UNOS. It is my understanding that Medicare depends on their certification of this program and also of the Joint Commission for the safe studying that's supposed to be insured for all Gift of Life patients.

Now, my findings have shown through surveys from CMS and the state, that this is not the case. I ask, why are certain facilities continuing to be approved? Why is the public not truly represented? Why is there not independent legal counsel available? And why is there not swift and right action afforded to the patients, loved ones, or caregivers, when the concerns are obvious and repugnant?

You have a facility that is allowed to operate in a monopolistic attitude. They own every avenue, including medical devices. They are allowed to import organs. As a representative to other communities, the concern for HIV strain in Cuba is a reality because the individual failures of their laboratory are shown through survey.

Dr. Barr: If I could make a recommendation Ms. Harty, if you could do us a favor and what you just expressed, if you could put this in the form of--

Ms. Harty: It's all been done, sir. Sir, it's all been done. And Mr. McLaughlin is very well aware of it, as is Mr. Walsh, as is Dr. Jim Bowman. All were notified in 2012. He knows, was told by me, by Dr. John Roberts, that the concerns represented, which, are still being found out, as shown in the March, the October 9 *Miami Herald* article about that failed OPO down there, that those concerns were represented to UNOS in 2012. Dr. Roberts told me that it would be presented before the membership committee, which apparently did nothing, as found by all CMS surveys.

Additionally, you may add in the fact that there appears to be nothing done in the proper, right, order. Your foundation is cracking, sir. And you are talking about progressing down the HIV corridor.

Ms. Stroup: Ms. Harty, we have to proceed to the next person. Thank you for your comment. If you put-

Ms. Harty: I think I've said enough. I'll be happy to hear from the Secretary. Thank you.

Ms. Stroup: Thank you very much. Do we have another public member to make a comment?

Mr. Morrison: Hi, this is Josh Morrison and I'd like to make a comment.

Dr. Barr: Yes, go ahead Josh. Josh if you can identify your organization.

Mr. Morrison: Hi, this is Josh Morrison on behalf of the Waitlist Zero. We are an organization representing living kidney donors and seeking to support living kidney donation. First, on behalf of living kidney donors, like myself, thank you to the advisory committee and to the people on this call for all your hard work. We all really appreciate it, and we know that this field didn't happen on its own. We definitely appreciate the hard work.

No additional comments were submitted.

Before declaring an end to the meeting, Dr. Barr reminded ACOT members and the public that the committee's next meeting, which will be a two-day, face-to-face event, will occur on May 10-11 in the Washington, D.C. area.

The meeting was adjourned.